

## AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning on page 1, line 6, as follows:

The present invention relates to a pharmaceutical composition containing as an active ingredient one or more HMG-CoA reductase inhibitor(s) for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract, and coronary artery disease), hypertension, obesity or arteriosclerosis; [[and]] or treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome, and

Please amend the paragraph beginning on page 1, line 21, as follows:

a method comprising administration of an effective amount of one or more HMG-CoA reductase inhibitor(s) to a warm-blooded animal for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract, and coronary artery disease), hypertension, obesity or arteriosclerosis; [[and]] or treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome.

LAW OFFICES OF  
CHRISTENSEN O'CONNOR JOHNSON KINDNESS<sup>PLLC</sup>  
1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100

Please amend the paragraph beginning on page 5, line 6, as follows:

On the basis of the above, a medicament that enhances adiponectin production has an action of improving insulin resistance and is useful as a pharmaceutical composition for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract, and coronary artery disease), hypertension, obesity or arteriosclerosis; ~~[[and]]~~ or treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome.

Please amend the paragraph beginning on page 6, line 25, as follows:

The inventors of the present invention found that an HMG-CoA reductase inhibitor has superior adiponectin production enhancing action, and is useful as a pharmaceutical composition for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract, and coronary artery disease), hypertension, obesity or arteriosclerosis; ~~[[and]]~~ or treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome, thereby leading to completion of the present invention.

LAW OFFICES OF  
CHRISTENSEN O'CONNOR JOHNSON KINDNESS<sup>LLC</sup>  
1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100

Please amend the paragraph beginning on page 7, line 8, as follows:

The present invention provides a pharmaceutical composition containing as an active ingredient one or more HMG-CoA reductase inhibitor(s), for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract, and coronary artery disease), hypertension, obesity or arteriosclerosis; [[and]] or treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome, and

Please amend the paragraph beginning on page 7, line 23, as follows:

a method comprising administration of an effective amount of one or more HMG-CoA reductase inhibitor(s) to a warm-blooded animal for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract, and coronary artery disease), hypertension, obesity or arteriosclerosis; [[and]] or treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome.

LAW OFFICES OF  
CHRISTENSEN O'CONNOR JOHNSON KINDNESS<sup>PC</sup>  
1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100

Please amend the paragraph beginning on page 8, line 8, as follows:

(2) a pharmaceutical composition as (1), wherein the HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin, lovastatin, simvastatin, fluvastatin, cerivastatin, atorvastatin, pitavastatin and rosuvastatin;

Please amend the paragraph beginning on page 8, line 16, as follows:

(4) a pharmaceutical composition as (1), wherein the HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 8, line 20, as follows:

(5) a pharmaceutical composition as (1), wherein the HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 8, line 29, as follows:

(8) a pharmaceutical composition as (7), wherein the water-soluble HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 9, line 1, as follows:

(9) a pharmaceutical composition as (7), wherein the water-soluble HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

LAW OFFICES OF  
CHRISTENSEN O'CONNOR JOHNSON KINDNESS<sup>PLC</sup>  
1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100

Please amend the paragraph beginning on page 9, line 10, as follows:

(12) a pharmaceutical composition as (11), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 9, line 15, as follows:

(13) a pharmaceutical composition as (11), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 9, line 25, as follows:

(16) a pharmaceutical composition as (15), wherein the HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin, lovastatin, simvastatin, fluvastatin, cerivastatin, atorvastatin, pitavastatin and rosuvastatin;

Please amend the paragraph beginning on page 9, line 33, as follows:

(18) a pharmaceutical composition as (15), wherein the HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 10, line 4, as follows:

(19) a pharmaceutical composition as (15), wherein the HMG-CoA reductase inhibitor is a ~~medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

LAW OFFICES OF  
CHRISTENSEN O'CONNOR JOHNSON KINDNESS<sup>PLLC</sup>  
1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100

Please amend the paragraph beginning on page 10, line 13, as follows:

(22) a pharmaceutical composition as (21), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 10, line 18, as follows:

(23) a pharmaceutical composition as (21), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 10, line 27, as follows:

(26) a pharmaceutical composition as (25), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 10, line 32, as follows:

(27) a pharmaceutical composition as (25), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 11, line 8, as follows:

(30) a pharmaceutical composition as (29), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

LAW OFFICES OF  
CHRISTENSEN O'CONNOR JOHNSON KINDNESS<sup>PC</sup>  
1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100

Please amend the paragraph beginning on page 11, line 13, as follows:

(31) a pharmaceutical composition as (29), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 11, line 26, as follows:

(34) a pharmaceutical composition as (33), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 11, line 31, as follows:

(35) a pharmaceutical composition as (33), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 12, line 10, as follows:

(38) a pharmaceutical composition as (37), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 12, line 15, as follows:

(39) a pharmaceutical composition as (37), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 12, line 29, as follows:

(43) a method as (41) or (42), wherein the HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin, lovastatin, simvastatin, fluvastatin, cerivastatin, atorvastatin, pitavastatin and rosuvastatin;

Please amend the paragraph beginning on page 13, line 4, as follows:

(45) a method as (41) or (42), wherein the HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin or a derivative thereof and rosuvastatin or a derivative thereof;

Please amend the paragraph beginning on page 13, line 8, as follows:

(46) a method as (41) or (42), wherein the HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 14, line 9, as follows:

(55) a method as any one of (48) to (54), wherein the water-soluble HMG-CoA reductase inhibitor is ~~a medicament~~ selected from the group consisting of pravastatin and rosuvastatin;

Please amend the paragraph beginning on page 23, line 6, as follows:

The HMG-CoA reductase inhibitor(s) serving as an active ingredient of the present invention is useful as a pharmaceutical composition for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery



disease), hypertension, obesity or arteriosclerosis; [[and]] or, treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome,

Please amend the paragraph beginning on page 23, line 20, as follows:

preferably for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; [[and]] or treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome,

Please amend the paragraph beginning on page 23, line 27, as follows:

more preferably for enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; [[and]] or treatment or prevention of diabetes or arteriosclerosis caused by hypoadiponectinemia,

Please amend the paragraph beginning on page 23, line 31, as follows:

and even more preferably for enhancement of adiponectin production [[and]] or treatment or prevention of hypoadiponectinemia.

Please amend the paragraph beginning on page 30, line 10, as follows:

From the aforementioned results, an HMG-CoA reductase inhibitor serving as an active ingredient of the present invention was found to enhance adiponectin production, to increase

insulin sensitivity and to enhance insulin-induced glucose uptake, and was determined to be useful as a pharmaceutical composition for the enhancement of adiponectin production; treatment or prevention of hypoadiponectinemia; improvement of insulin resistance; treatment or prevention of Syndrome X or metabolic syndrome; treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis; [[and]] or the treatment or prevention of diabetes, diabetes complications (including retinopathy, nephropathy, neuropathy, cataract and coronary artery disease), hypertension, obesity or arteriosclerosis caused by hypoadiponectinemia or insulin resistance syndrome.

LAW OFFICES OF  
CHRISTENSEN O'CONNOR JOHNSON KINDNESS<sup>PC</sup>  
1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100